SEQUENCE LISTING

- <110> Zankel et al.
- <120> MEGALIN-BASED DELIVERY OF THERAPEUTIC COMPOUNDS TO THE BRAIN AND OTHER TISSUES
- <130> 30610/40037
- <140> To be assigned
- <141> 2004-03-30
- <150> US 10/600,862
- <151> 2003-06-20
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- <170> PatentIn version 3.2
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Glu Glu Ile His Glu Asn Val Ile Ser Pro Ser Asp Leu Ser Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr Glu Leu Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Arg Val Ser His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu Pro Arg Val Ile Asp Leu 105 Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr Asp Lys Glu Leu Glu Ala 120 Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile Glu Lys His Asn 130 135 His Tyr Gln Lys Gln Leu Glu Ile Ala His Glu Lys Leu Arg His Ala 145 150 155 Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser Arg Glu Lys His. 165 Ala: Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr Thr Val Lys Lys 180 185 His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala Arg His Asn Glu Leu <210> 3 <211> 33 <212> DNA <213> Artificial sequence <220> <223> Synthetic primer ccgcgtggat cccccaggct ggaaaagctg tgg 33

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Tyr Glu Asn Leu Leu Ser Pro Ser Asp Met Thr His Ile Lys Ser Asp 55

Thr Leu Ala Ser Lys His Ser Glu Leu Lys Asp Arg Leu Arg Ser Ile

Asn Gln Gly Leu Asp Arg Leu Arg Lys Val Ser His Gln Leu Arg Pro

Ala Thr Glu Phe Glu Glu Pro Arg Val Ile Asp Leu Trp Asp Leu Ala

Gln Ser Ala Asn Phe Thr Glu Lys Glu Leu Glu Ser Phe Arg Glu Glu

Leu Lys His Phe Glu Ala Lys Ile Glu Lys His Asn His Tyr Gln Lys 130

Gln Leu Glu Ile Ser His Gln Lys Leu Lys His Val Glu Ser Ile Gly 145

Asp Pro Glu His Ile Ser Arg Asn Lys Glu Lys Tyr Val Leu Leu Glu

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Glu Thr Leu Ser Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro 180 185 190

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955

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- His Val Ala Gly Glu Thr Val Ala Arg Pro Leu Phe Leu Glu Phe Pro 995 1000 1005
 - Lys Asp Ser Ser Thr Trp Thr Val Asp His Gln Leu Leu Trp Gly 1010 1015 1020
 - Glu Ala Leu Leu Ile Thr Pro Val Leu Gl
n Ala Gly Lys Ala Glu 1025 1030 1035
 - Val Thr Gly Tyr Phe Pro Leu Gly Thr Trp Tyr Asp Leu Gln Thr 1040 1045 1050
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Gly	Tyr	Thr	Val	Lys 325	Lys	His	Leu	Gln	Asp 330	Leu	Ser	Gly	Arg	Ile 335	Ser
Arg	Ala	Arg	Ala 340	Glu	Ala	Glu	Thr	Gly 345	Glu	Ala	Pro	His	Leu 350	Val	His
Val	Asp	Ala 355	Ala	Arg	Aļa	Leu	Trp 360	Pro	Leu	Arg	Arg	Phe 365	Trp	Arg	Ser
Thr	Gly 370	Phe	Суѕ	Pro	Pro	Leu 375	Pro	His	Ser	Gln	Ala 380	Asp	Gln	Tyr	Val
Leu 385	Ser	Trp	Asp	Gln	Gln 390	Leu	Asn	Leu	Ala	Tyr 395	Val	Gly	Ala	Val	Pro 400
His	Arg	Gly	Ile	Lys 405	Gln	Val	Arg	Thr	His 410	Trp	Leu	Leu	Glu	Leu 415	Val
Thr	Thr	Arg	Gly 420	Ser	Thr	Gly	Arg	Gly 425	Leu	Ser	Tyr	Asn	Phe 430	Thr	His
Leu	Asp	Gly 435	Tyr	Leu	Asp	Leu	Leu 440	Arg	Glu	Asn	Gln	Leu 445	Leu	Pro	Gly
Phe	Glu 450	Leu	Met	Gly	Ser	Ala 455	Ser	Gly	His	Phe	Thr 460	Asp	Phe	Glu	Asp
Lys 465	Gln	Gln	Val	Phe	Glu 470	Trp	Lys	Asp	Leu	Val 475	Ser	Ser	Leu	Ala	Arg 480
Arg	Tyr	Ile	Gly	Arg 485	Tyr	Gly	Leu	Ala	His 490	Val	Ser	Lys	Trp	Asn 495	Phe
Glu	Thr	Trp	Asn 500	Glu	Pro	Asp	His	His 505	Asp	Phe	Asp	Asn	Val 510	Ser	Met

	Thr Met	GIN G. 515	ly Phe	Leu As	520	Tyr	Asp	Ala	Cys	525	Glu	GIÀ	Leu		
	Arg Ala 530	Ala Se	er Pro		eu Arg 85	Leu	Gly	Gly	Pro 540	Gly	Asp	Ser	Phe		
	His Thr 545	Pro P	ro Arg	Ser Pr 550	co Leu	Ser	Trp	Gly 555	Leu	Leu	Arg	His	Cys 560		
٠	His Asp	Gly T	hr Asn 565	Phe Pl	ne Thr	Gly	Glu 570	Ala	Gly	Val	Arg	Leu 575	Asp	·	
	Tyr Ile	51	eu His 80	Arg Ly	s Gly	Ala 585	Arg	Ser	Ser	Ile	Ser 590	Ile	Leu		
٠	Glu Gln	Glu Ly 595	ys Val	Val A	la Gln 600	Gln	Ile	Arg	Gln	Leu 605	Phe	Pro	Lys		
	Phe Ala 610	Asp T	hr Pro		r Asn 15	Asp	Glu	Ala	Asp 620	Pro	Leu	Val	Gly		
:	Trp Ser 625	Leu P	ro Gln	Pro T: 630	rp Arg	Ala	Asp	Val 635	Thr	Tyr	Ala	Ala	Met 640		
	Val Val	Lys V	al Ile 645	Ala G	ln His	Gln	Asn 650	Leu	Leu	Leu	Ala	Asn 655	Thr		
	Thr Ser		he Pro 60	Tyr A	la Leu	Leu 665	Ser	Asn	Asp ·	Asn	Ala 670	Phe	Leu		
٠	Ser Tyr	675		•	680					685					
	Gln Val 690			6	95		-		700		_	-			
	Val Leu 705			710				715	_				720		
٠	Trp Ala		725				730					735			
	Val Gly	7-	40			745			-		750	_			
	Trp Arg	Ala A 755	ıa Val	Leu I	le Tyr 760		Ser	Asp	Asp	Thr 765	Arg	Ala	Hıs		

Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro 770 775 780

Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu Cys

Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro Thr 805 810 815

Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala Ala 820 825 830

Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro Ala 835 840 845

Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro Glu 850 855 860

Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln 865 870 875 880

Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys 885 890 895

Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr Thr 900 905 910

Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser Pro 915 920 925

Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp Tyr 930 935 940

Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu Val 945 950 955 960

Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro 965 970

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<211> 1398

<212> DNA

<213> Artificial sequence

<220>

<223> RAP-GDNF fusion sequence

<400> 10

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                                                                      120
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                                                                      180
ctcgcctgga agaaactaaa gcttgacggc ttggacgaag atggggagaa ggaagcgaga
                                                                      240
ctcatacgca acctcaatgt catcttggcc aagtatggtc tggacggaaa gaaggacgct
                                                                      300
eggeaggtga ceageaacte ceteagtgge acceaggaag aegggetgga tgaceeeagg
                                                                      360
ctggaaaagc tgtggcacaa qgcgaaqacc tctqqqaaat tctccqqcqa aqaactqqac
                                                                      420
aagetetgge gggagtteet geateaeaaa gagaaagtte aegagtaeaa egteetgetg
                                                                      480
gagaccetga geaggacega agaaateeae gagaaegtea ttageeeete ggaeetgage
                                                                      540
gacatcaagg gcagcgtcct gcacagcagg cacacggagc tgaaggagaa gctgcgcagc
                                                                      600
atcaaccagg geetggaceg eetgegeagg gteagecace agggetacag caetgagget
                                                                      660
gagttcgagg agcccagggt gattgacctg tgggacctgg cgcaqtccqc caacctcacq
                                                                      720
gacaaggagc tggaggcgtt ccgggaggag ctcaagcact tcgaagccaa aatcgagaag
                                                                      780
cacaaccact accagaagca gctggagatt gcgcacgaga agctgaggca cgcagagagc
                                                                      840
gtgggcgacg gcgagcgtgt gagccgcagc cgcgagaagc acgccctgct ggaggggcgg
                                                                      900
accaaggage tgggetacae ggtgaagaag catetgeagg acctgteegg caggatetee
                                                                      960
agageteggg eegaggeaga aaceggttea eeagataaac aaatggeagt getteetaga
                                                                     1020
agagagegga ateggeagge tgeagetgee aacceagaga attecagagg aaaaggtegg
                                                                     1080 '
agaggccaga ggggcaaaaa ccggggttgt gtcttaactg caatacattt aaatgtcact
                                                                     1140
gacttgggtc tgggctatga aaccaaggag gaactgattt ttaggtactg cagcgqctct
                                                                     1200
tgcgatgcag ctgagacaac gtacgacaaa atattgaaaa acttatccag aaatagaagg
                                                                     1260
ctggtgagtg acaaagtagg gcaggcatgt tgcagaccca tcgcctttga tgatgacctg
                                                                     1320
tcgtttttag atgataacct ggtttaccat attctaagaa agcattccgc taaaaggtgt
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Lys Arg Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu 20 25 30

<211> 463

<212> PRT

<213> Artificial sequence

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<223> RAP-GDNF fusion sequence

<400> 11

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 Leu His Ala Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu Ala Trp Lys
- Lys Leu Lys Leu Asp Gly Leu Asp Glu Asp Gly Glu Lys Glu Ala Arg 65 70 75 80

55

- Leu Ile Arg Asn Leu Asn Val Ile Leu Ala Lys Tyr Gly Leu Asp Gly 85 90 95
- Lys Lys Asp Ala Arg Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln
 100 105 110
- Glu Asp Gly Leu Asp Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala 115 120 125
- Lys Thr Ser Gly Lys Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg 130 135 140
- Glu Phe Leu His His Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu 145 150 155 160
- Glu Thr Leu Ser Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro 165 170 175
- Ser Asp Leu Ser Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr 180 185 190
- Glu Leu Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu 195 200 205
- Arg Arg Val Ser His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu 210 220
- Pro Arg Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr 225 230 235 240
- Asp Lys Glu Leu Glu Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala 245 250 255
- Lys Ile Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His 260 265 270
- Glu Lys Leu Arg His Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser 275 280 285

Arg Ser Arg Glu Lys His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr Thr Val Lys Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser 305 310 Arg Ala Arg Ala Glu Ala Glu Thr Gly Ser Pro Asp Lys Gln Met Ala 325 Val Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala Ala Asn Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly Ser 390 395 Cys Asp Ala Ala Glu Thr Thr Tyr Asp Lys Ile Leu Lys Asn Leu Ser 410 Arg Asn Arg Arg Leu Val Ser Asp Lys Val Gly Gln Ala Cys Cys Arg 420 425 Pro Ile Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu Val 445 Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys Ile • 450 460 455 <210> 12 <211> 49 <212> DNA <213> Artificial sequence <220> <223> Synthetic primer <400> 12 gcgataggat cctactcgcg ggagaagaac cagcccaagc cgtccccga 49 <210> 13 <211> 57 <212> DNA <213> Artificial sequence

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<212> DNA
<213> Artificial sequence
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<223> Synthetic primer
<400> 14
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<210> 15
<211> 37
<212> DNA
<213> Artificial sequence
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<223> Synthetic primer
<400> 15
gcgatactcg agtcaacacc agctgacgag aaactgc
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      16
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      46
<212>
      DNA
<213> Artificial sequence
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      Synthetic primer
<400> 16
gcgataaccg gtgaggcccc ccgcacctgg tgcatgtgga cgcggc
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<210> 17
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<212> DNA
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<400> 18
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<210><211><212><213>	21 357 PRT Homo	sap	iens												
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Met Al	a Pro	Arg	Arg 5	Val	Arg	Ser	Phe	Leu 10	Arg	Gly	Leu	Pro	Ala 15	Leu	
Leu Le	u Leu	Leu 20	Leu	Phe	Leu	Gly	Pro 25	Trp	Pro	Ala	Ala	Ser 30	His	Gly	
Gly Ly	s Tyr 35	Ser	Arg	Glu	Lys	Asn 40	Gln	Pro	Lys	Pro	Ser 45	Pro	Lys	Arg	
Glu Se	r Gly	Glu	Glu	Phe	Arg 55	Met	Glu	Lys	Leu	Asn 60	Gln	Leu	Trp	Glu	
Lys Al		Arg	Leu	His 70	Leu	Pro	Pro	Val	Arg 75	Leu	Ala	Glu	Leu	His 80	
Ala As	p Leu	Lys	Ile 85	Gln	Glu	Arg	Asp	Glu 90	Leu	Ala	Trp	Lys	Lys 95	Leu	
Lys Le	u Asp	Gly 100	Leu	Asp	Glu	Asp	Gly 105	Glu	Lys	Glu	Ala	Arg 110	Leu	Ile	
Arg As:	n Leu	Asn	Val	Ile	Leu	Ala	Lys	Tyr	Gly	Leu	Asp	Gly	Lys	Lys	

Asp Ala Arg Gln Val Thr Ser Asn Ser Leu Ser Gly Thr Gln Glu Asp 135 Gly Leu Asp Asp Pro Arg Leu Glu Lys Leu Trp His Lys Ala Lys Thr 145 150 155 Ser Gly Lys Phe Ser Gly Glu Glu Leu Asp Lys Leu Trp Arg Glu Phe 165 170 Leu His His Lys Glu Lys Val His Glu Tyr Asn Val Leu Leu Glu Thr 180 185 Leu Ser Arg Thr Glu Glu Ile His Glu Asn Val Ile Ser Pro Ser Asp Leu Ser Asp Ile Lys Gly Ser Val Leu His Ser Arg His Thr Glu Leu 215 Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Arg Val Ser His Gln Gly Tyr Ser Thr Glu Ala Glu Phe Glu Glu Pro Arg Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala Asn Leu Thr Asp Lys Glu Leu Glu Ala Phe Arg Glu Glu Leu Lys His Phe Glu Ala Lys Ile 275 Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ala His Glu Lys 290 295 Leu Arg His Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser 305 Arg Glu Lys His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr 325

Thr Val Lys Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala

345

Arg His Asn Glu Leu 355

<210> 22

<211> 378

<212> PRT

<213> Mus musculus

<400> 22

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Met Gly Gly Pro Thr Arg Pro Ser Pro Val Ser Leu Leu Ala Leu Gln 1 · 5 10 15

Arg Lys Met Ala Pro Arg Arg Glu Arg Val Ser Thr Leu Pro Arg Leu
20 25 30

Gln Leu Val Leu Leu Leu Leu Pro Leu Met Leu Val Pro Gln Pro 35 40 45

Ile Ala Gly His Gly Gly Lys Tyr Ser Arg Glu Lys Asn Glu Pro Glu
50 60

Met Ala Ala Lys Arg Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu 65 70 75 80

Asn Gln Leu Trp Glu Lys Ala Lys Arg Leu His Leu Ser Pro Val Arg 85 90 95

Leu Ala Glu Leu His Ser Asp Leu Lys Ile Gln Glu Arg Asp Glu Leu 100 105 110

Asn Trp Lys Lys Leu Lys Val Glu Gly Leu Asp Lys Asp Gly Glu Lys 115 120 125

Glu Ala Lys Leu Ile His Asn Leu Asn Val Ile Leu Ala Arg Tyr Gly 130 135 140

Leu Asp Gly Arg Lys Asp Ala Gln Met Val His Ser Asn Ala Leu Asn 145 150 155 160

Glu Asp Thr Gln Asp Glu Leu Gly Asp Pro Arg Leu Glu Lys Leu Trp 165 170 175

His Lys Ala Lys Thr Ser Gly Lys Phe Ser Ser Glu Glu Leu Asp Lys 180 185 190

Leu Trp Arg Glu Phe Leu His Tyr Lys Glu Lys Ile Gln Glu Tyr Asn 195 200 205

Val Leu Leu Asp Thr Leu Ser Arg Ala Glu Glu Gly Tyr Glu Asn Leu 210 215 220

Leu Ser Pro Ser Asp Met Ala His Ile Lys Ser Asp Thr Leu Ile Ser Lys His Ser Glu Leu Lys Asp Arg Leu Arg Ser Ile Asn Gln Gly Leu Asp Arg Leu Arg Lys Val Ser His Gln Gly Tyr Gly Ser Thr Thr Glu 265 Phe Glu Glu Pro Arg Val Ile Asp Leu Trp Asp Leu Ala Gln Ser Ala 280 Asn Phe Thr Glu Lys Glu Leu Glu Ser Phe Arg Glu Glu Leu Lys His 295 Phe Glu Ala Lys Ile Glu Lys His Asn His Tyr Gln Lys Gln Leu Glu Ile Ser His Gln Lys Leu Lys His Val Glu Ser Ile Gly Asp Pro Glu 325 335 His Ile Ser Arg Asn Lys Glu Lys Tyr Val Leu Leu Glu Glu Lys Thr Lys Glu Leu Gly Tyr Lys Val Lys Lys His Leu Gln Asp Leu Ser Ser 355 360 Arg Val Ser Arg Ala Arg His Asn Glu Leu 370 375 <210> 23 <211> 357 <212> PRT <213> Rat <400> 23 Leu Arg Asp Arg Val Ser Thr Leu Pro Arg Leu Gln Leu Leu Val Leu Leu Leu Pro Leu Leu Val Pro Gln Pro Ile Ala Gly His Gly Gly Lys Tyr Ser Arg Glu Lys Asn Glu Pro Glu Met Ala Ala Lys Arg Glu Ser Gly Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu Trp Glu

65	ніа	гур	AIG	ьeu	70	Leu	ser	PIO	vai	75	Leu	Ala	GIU	ьеи	80
Ser	Asp	Leu	Lys	Ile 85	Gln	Glu	Arg	Asp	Glu 90	Leu	Asn	Trp	Lys	Lys 95	Leu
Lys	Val	Glu	Gly 100	Leu	Asp	Gly	Asp	Gly 105	Glu	Lys	Glu	Ala	Lys 110	Leu	Val
His	Asn	Leu 115	Asn	Val	Ile	Leu	Ala 120	Arg	Tyr	Gly	Leu	Asp 125	Gly	Arg	Lys
Asp	Thr 130	Gln	Thr	Val	His	Ser 135	Asn	Ala	Leu	Asn	Glu 140	Asp	Thr	Gln	Asp
Glu 145	Leu	Gly _.	Asp	Pro	Arg 150	Leu	Glu	Lys	Leu	Trp 155	His	Lys	Ala	Lys	Thr 160
		_		165					170		•		Arg	175	
			180					185					Leu 190		
		195					200		•			205	Pro		
	210				٠	215					220		Ser		
225					230					235	_		Leu		240
				245					250	-			Glu	255	
			260					265			•		Thr 270		
		275					280					285	Ala	_	
	290				_	295					300				
305	пÄg	птв	val	GIU	310	116	GIÀ	Asp	Pro	315	HIS	тте	Ser	arg	320

Lys Glu Lys Tyr Val Leu Leu Glu Glu Lys Thr Lys Glu Leu Gly Tyr 325 330 335

Lys Val Lys Lys His Leu Gln Asp Leu Ser Ser Arg Val Ser Arg Ala 340 345 350

Arg His Asn Glu Leu 355

<210> 24

<211> 348

<212> PRT

<213> Chicken

<400> 24

Met Gly Ala Thr Arg Thr Leu Val Ala Val Met Ala Ala Phe Leu Ala 1 5 10 15

Val Ser Thr Arg Ala Ser Lys Tyr Thr Arg Glu Ala Asn Glu Gly Leu 20 25 30

Ala Asp Ala Lys Arg Arg Glu Ala Gly Glu Phe Arg Val Val Arg Leu 35 40 . 45

Asn Gln Val Trp Glu Lys Ala Gln Arg Leu Gln Leu Ser Ala Val Lys
50 55 60

Leu Ala Glu Leu His Ser Asp Leu Lys Ile Gln Glu Lys Asp Glu Leu 65 70 75 80

Ser Trp Lys Lys Leu Lys Ala Glu Gly Leu Gly Glu Asp Gly Glu Lys 85 90 95

Glu Ala Lys Leu Arg Arg Asn Ile Asn Val Ile Met Thr Lys Tyr Gly
100 105 110

Met Asn Gly Lys Lys Asp Ser His Leu Thr Asp Thr Asn Tyr Ile Lys 115 120 125

Asp Gly Thr Glu Ser Asp Thr Leu Asp Asp Pro Arg Leu Glu Lys Leu 130 135 140 .

Trp Ser Lys Ala Lys Thr Ser Gly Lys Phe Ser Asp Glu Glu Leu Asp 145 150 155 160

Lys Leu Trp Arg Glu Phe Lys His His Lys Glu Lys Ile Arg Glu Tyr 165 170 175 Asn Ile Leu Leu Glu Thr Val Ser Arg Thr Glu Asp Ile His Lys Lys 180 185 190

Val Ile Asn Pro Ser Glu Glu Asn Pro Val Lys Glu Glu Val Leu His 195 200 205

Asn Lys His Arg Glu Leu Lys Glu Lys Leu Arg Ser Ile Asn Gln Gly 210 215 220

Phe Glu Arg Leu Arg Lys Val Ser His Gln Gly Tyr Asp Ala Thr Ser 225 230 235 240

Glu Phe Glu Glu Pro Arg Val Ile Asp Leu Trp Asp Met Ala Lys Ser 245 250 255

Ala Asn Phe Thr Glu Lys Glu Leu Glu Ser Phe Arg Glu Glu Leu Lys
260 265 270

His Phe Glu Ala Lys Ile Glu Lys His His Tyr Gln Lys Gln Leu 275 280 285

Glu Ile Ser His Glu Lys Leu Lys His Ile Glu Gly Thr Gly Asp Lys 290 295 300

Glu His Leu Asn Arg Asn Arg Glu Lys Tyr Ala Met Leu Glu Glu Lys 305 310 315 320

Thr Lys Glu Leu Gly Tyr Lys Val Lys Lys His Leu Gln Asp Leu Ser 325 330 335

Ser Arg Ile Ser Gln Gly Leu Gln His Asn Glu Leu 340 345

<210> 25

<211> 331

<212> PRT

<213> Zebrafish

<400> 25

Met Ala Gly Lys Tyr Ser Lys Glu Met Asn Glu Lys Asn Ala Ser Asp 1 5 10 15

Lys Ser Asn Asn Gln Val Glu Phe Arg Ile Ala Lys Leu Asn Gln Val 20 25 30

Trp Glu Lys Ala Ile Arg Met Gln Leu Ala Pro Val Arg Leu Ser Glu 35 40 45

Leu His Ser Asp Leu Lys Ile Gln Glu Lys Asp Glu Leu Gln Trp Lys Lys Leu Lys Ala Glu Gly Met Asp Glu Asp Gly Glu Arg Glu Ala Lys Leu Arg Arg Asn Phe Asn Ile Ile Leu Ala Lys Tyr Gly Met Asp Gly Lys Lys Asp Thr Arg Thr Leu Asp Ser Asn Arg Leu Lys Asp His Glu Val Lys Ile Gly Asp Thr Phe Asp Asp Pro Lys Leu Asp Lys Leu Trp 120 Asn Lys Ala Arg Thr Ser Gly Lys Phe Ser Asp Glu Glu Leu Gln Thr 130 135 Leu His Arg Glu Phe Gln His His Lys Asp Lys Ile His Glu Tyr Asn 150 . 155 Ile Val Met Asp Thr Val Ser Arg Thr Glu Glu Ile His Lys Asn Val 165 Ile Ser Pro Leu Glu Gly Asp Val Lys Glu Asn Val Leu His Gln Lys 180 185 190 His Thr Asp Leu Lys Gln Arg Met Arg Asp Leu Asn Gln Gly Phe Glu Arg Leu Arg Lys Ile Thr His Glu Gly Tyr Thr Asp Asp Ser Glu Phè 210 215 220 Arg Glu Pro Arg Val Ile Glu Leu Trp Glu Met Ala Lys Arg Ser Asn Leu Ser Glu Asp Glu Leu Asp Ser Leu Lys Glu Glu Leu Arg His Phe Glu Thr Lys Val Glu Lys His Gln His Tyr Gln Glu Gln Leu Glu Leu

Ser His Gln Lys Leu Lys His Val Glu Ala Leu Gly Asp Glu Asp His

Ile Met Arg Asn Lys Glu Lys Tyr Asn Thr Leu Ala Glu Lys Ala Arg

280

295

275

290

Glu Met Gly Tyr Lys Met Lys Lys His Leu Gln Asp Leu Thr Asn Lys 305 310 315 320

Leu Ser Lys Asn Gly Leu Gln His Asn Glu Leu 325 330

<210> 26

<211> 379

<212> PRT

<213> Fruit fly

<400> 26

Met Val Arg Ser Ala Leu Val Val Ala Ala Ile Ala Leu Ser Val Leu

1 10 15

Ile Ala Leu Gln Gly Val Asp Ala Asp Lys Lys Gln Ser Lys Lys Tyr
20 25 30

Ser Lys Glu Ala Asn Asp Pro His Phe Gln Gln Val Lys Gln Glu Lys
35 40 45

Tyr Asp Pro Asp Phe Lys Ser Ile Gln Arg Pro Phe Arg Met Ala Lys 50 55 60

Leu Asn Leu Val Trp Ala Lys Ala Gln Asn Arg Leu Thr Glu Pro Lys 70 75 . 80

Leu Lys Ser Leu Tyr Met Glu Leu Lys Ile His Asp Lys Glu Glu Ile 85 90 95

Ala Trp Lys Gln Leu Asn Ser Gln His Lys Asp Lys Asp Gly Leu Lys
100 105 110

Ala Asp Glu Leu Arg Arg Lys Leu Ile Gly Ile Met Ser Ser Tyr Asp 115 120 125

Leu Leu Glu His Phe Asp Asp Thr Gln Asp Thr Glu Lys Leu Lys Pro 130 135 140

Tyr Lys Lys Phe His Asp Ala Glu Glu Arg His Arg Asn Lys Ser Leu 145 . 155 . 160

Phe Lys Asp Lys Leu Asn Arg Leu Trp Glu Lys Ala Glu Ile Ser 165 170 175

Gly Phe Thr Ala Glu Glu Leu Lys Ser Leu Lys Gln Glu Phe Asp His 180 185 190 His Gln Asp Lys Val Asp Val Tyr Tyr Ser Leu Leu Glu Asn Ile Gly 195 200 205

Thr Val Asp Thr Asp Lys His Glu Asn Ala Ile Asn Thr Glu Asp Leu 210 215 220

Asp Thr Tyr Asn Leu Ile Ser Asn Asp Val Asn Glu Asn Asp Ile Lys 225 230 235 240

Thr His Ala Gln Asn Val Lys Ser Phe Glu Asn Asp Leu Asn Thr Leu 245 250 255

Arg Gly His His Thr Gly Ile Lys Asp His Tyr Asp Arg Leu Glu Arg 260 265 270

Leu Val Ser Ser Gly Pro His Ser Gln Asp Phe Ile Glu Pro Lys Val 275 280 285

Gln Gly Leu Trp Arg Val Ala Gln Ala Ser Asn Phe Thr Val Lys Glu 290 295 300

Leu Glu Ser Ile Lys Thr Glu Leu His His Phe Glu Ser Arg Leu Leu 305 310 315 320

Lys Leu Arg His Leu His Ala Glu His Ala Leu Gln Lys Glu Lys Tyr 325 330 335

Lys Gly Glu Lys Val Lys Asp Lys Ser Ser Arg Phe Glu Glu Met Glu 340 345 350

Asp Gln Leu Lys Lys Gln Thr Arg Lys Val Glu Lys Leu Gln Glu Asn 355 360 365

Ile Glu Lys Thr Ile Phe Lys His Thr Glu Leu 370 375

<210> 27

<211> 400

<212> PRT

<213> Mosquito

<400> 27

Glu Leu Cys Pro Ile Ala Arg Arg Lys Arg Gly Ile Lys His Thr Leu
1 5 10 15

Thr Met Pro Leu Phe Thr Arg Leu Cys Val Ile Val Phe Thr Val Leu 20 25 30

- Val Cys Asn His Val Val Gln Ser Glu Lys Ala His Ser Lys Tyr Ser Lys His Ala Asn Ala Leu Pro Asp Ser Glu Ile Tyr Glu Pro Asp Phe Arg Asn Ile Gln Arg Pro Phe Arg Met Ala Lys Leu Asn Leu Val Trp 75 Thr Lys Ala Gln His Arg Leu Thr Glu Pro Lys Leu Lys Ser Leu Tyr Thr Glu Leu Lys Leu His Asp Lys Glu Glu Leu Thr Tyr Lys Gln Leu 105 Lys Glu Lys Asp Lys Asp Gly Leu Lys Glu Ala Glu Leu Arg Asn Lys 115 Leu Val Ser Ile Met Ser Thr Tyr Gly Leu Leu Glu His Phe Asp Asp 130 135 140 Thr Gln Asp Pro Glu Lys Tyr Lys Leu Ala Lys Ser Ser Asp Gly Ala 145 Pro Lys Lys Asp Thr Tyr Lys Asn Lys Ser Leu Phe Lys Asp Lys Lys 165 170 Leu Asn Lys Leu Trp Asp Lys Ala Glu Ser Ala Gly Phe Thr Lys Glu Glu Leu Asp Ala Leu Arg Glu Glu Phe Asp His His Gln Ala Lys Ile 195 200 Asp Val Tyr Tyr Ser Leu Leu Glu Arg Leu Gly Asp Asp Asp Asp Gly
- Ala Val Asn Asp Glu Glu His Asp Arg Tyr Asn Glu Val Asp Arg Ala 245 250 255

Gly Ala Ala Gly Gln Gly Ser Arg Arg Asp Asp Ala Leu Leu Asn

- Glu Glu Thr Asp Arg Ser Gln Pro Gly Ala Asn Lys Gln His Ala Tyr 260 265 270
- Leu His Lys Ser Asn Gln Leu Arg Glu Lys His Arg Glu Ile Arg Asp 275 280 285

Asn Phe Asp Arg Leu Asp Arg Ile Ala Ser Lys Gly Pro Lys Ser Gln 290 295 300

Asp Phe Val Glu Pro Lys Val Gln Gly Leu Trp Arg Val Ala Leu Ala 305 310 315 320

Ser Asp Phe Ser Ala Asp Glu Leu Ala Ser Leu Lys Val Glu Leu Leu 325 330 335

His Tyr Glu Ser Arg Leu Leu Lys Leu Arg His Met His Ala Glu His 340 345 350

Ala Leu Ser Leu Glu Lys His Lys His Ser Asp Ala Lys Ala Asp Thr 355 360 365

His Lys Leu Met Glu Asp Asn Ile Lys Lys Gln Thr Arg Lys Val Glu 370 375 380

Lys Met Gln Glu Glu Val Glu Arg Arg Ile Phe Lys His Ser Glu Leu 385 390 395 400

<210> 28

<211> 331

<212> PRT

<213> Flatworm

<400> 28

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Tyr Glu Lys Ala Leu Gln His Val Thr Asp Arg Gln Asn Leu Ala Arg 35 40 45

Leu Glu Lys Glu Leu Ser Gly Tyr Asp Ala Ile Tyr Leu Ala Ser Lys 50 55 60

Ser Asn Arg Gln Gly Thr Gln Gly Thr Lys Glu Ile Asp Lys Ile Asp 65 70 75 80

Asp Lys Leu Gly Lys Ile Leu Glu Lys Tyr Gly Leu Glu Lys Ala Val 85 90 95

Leu Ala Phe Lys Glu Lys Tyr Lys His Lys Asn Leu Phe Gln Gln Thr 100 105 110

Gln Lys Leu Trp Ser Gln Ala Gln Asn Gly Lys Phe Ser Gln Lys Glu Leu Asn Ala Leu His Gly Glu Leu Lys Glu Val Glu Gln Lys Met Arg 150 Val Tyr Glu Asp Gln Leu Asp Asp Phe Lys Lys Val Pro His Glu Asn 170 Ser Ile Gln His Asp Ile Glu Ser Ile Gly Asp Lys Thr Lys Lys Leu 185 Lys Ala Ala Asn Arg Glu Leu Asn Asp His Leu Asp Glu Val His Arg Lys Val Thr Ser Glu Glu Phe Ser Pro Phe Asn Glu Pro Arg Val Lys . 210 215 220 Arg Leu Trp Lys Leu Ala Gln Glu Asn Glu Lys Leu Thr Pro His Glu 225 230 235 Leu Ser Val Leu Lys Asp Glu Leu Ser His Phe Glu Ser Gln Leu Lys 245 250 Lys Ile Glu Phe His Lys Val Phe Phe Val Ala Asn Ser Cys Pro Lys Arg Gly Lys Asn Glu Glu Val Ser Arg Leu Gln Glu Asp Ala Glu 275 280 Glu Arg Gly Lys Asp Lys Ser Gln Val Tyr Glu Asn Leu Glu Leu Ser Ile Lys His Glu Lys Leu Asn Arg Lys Ala Arg Lys Leu Glu Lys Tyr 315

Asp Asp Asn Glu Pro Leu Pro Ser Gly Lys Phe Thr Asp Gln Asn Leu

<210> 29

<211> 6

<212> PRT

<213> Artificial sequence

Ile Glu Glu Lys Ile Ile His Arg Glu Leu

<220>

<223> Synthetic peptide

<400> 29

Ala Glu Ala Glu Thr Gly